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EXAMINER	
BALASUBRAMANIAN, VENKATARAMAN	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,941	STOKES ET AL.	
	Examiner	Art Unit	
	/Venkataraman Balasubramanian/	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-11,16 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-11, 16 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' response, which included cancellation of claims 2, 12, 14, addition of new claim 18 and amendment to claims 1, 8-11 and 16, filed on 1/10/2008, is made of record. Claims 1, 3-11, 16 and 18 are now pending. In view of applicants' response, all 112 second paragraph rejections made in the previous office action have been obviated. However, the following rejections are applied to currently pending claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 16 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating breast cancer does not reasonably provide enablement for all or any diseases including any or all cancer by inhibiting HDAC generically embraced in the claim language. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Following reasons apply.

Instant claim 16 is drawn to inhibiting HDAC while claim 16 is drawn to treating cancer in general. Claim 16 is a reach through claim. A reach through claim is a claim drawn to a mechanistic, receptor binding or enzymatic functionality in general format and thereby reach through a scope of invention for which they lack adequate written description and enabling disclosure in the specification.

In the instant case claim 16, based on the inhibition of HDAC by the instant compounds, reach through treatment any or all cancers and thereby they lack adequate written description and enabling disclosure in the specification.

More specifically, in the instant case, based on the mode of action of instant compounds as inhibitor of HDAC activity, based on limited assay, it is claimed that the instant compounds are useful for treating of any or all cancers in general, for which there is no adequate written description and enabling disclosure in the instant specification.

In addition, the scope of claim16 includes treatment of various cancers in general. The scope of the term cancer would include lung cancer, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region. stomach cancer, colon cancer, breast cancer, uterine cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin's disease, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, prostate cancer, chronic or acute leukemia, lymphocytic lymphomas, cancer of the bladder, cancer of the kidney or ureter, renal cell carcinoma, carcinoma of the renal pelvis, neoplasms of the central nervous system (CNS), primary CNS lymphoma, spinal axis tumors, brain stem glioma, pituitary adenoma, or a

combination of one or more of the foregoing cancers, which is not adequately enabled solely based on the activity of the compounds provided in the specification.

Applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the uses disclosed and embraced by the claim language for the intended host. Moreover many if not most of diseases such as lung cancer, brain cancer, pancreatic cancer, colon cancer etc. are very difficult to treat and despite the fact that there are many anticancer agents.

The scope of the claims involves millions of compounds of claim 1 as well as the thousands of cancers embraced by the term cancer. No compound has ever been found to treat diseases of all types generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "compound" is contrary to our present understanding of modern medicine. For example, as for cancer, Cecil Textbook of Medicine states, "each specific type has unique biologic and clinical features that must be appreciated for proper diagnosis, treatment and study" (see the enclosed article, page 1004). Different types of cancers affect different organs and have different methods of growth and harm to the body. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally.

Also see the PTO website

<<http ://www.uspto.gov/web/offices/pac/dapp/1 pecba.htm#7>>

ENABLEMENT DECISION TREE, Example F, situation 1) which is directed to the scope of cancers.

Additionally, cell line testing is not a reliable guide for in vivo treatment since such testing has historically failed to produce a proportionate number of compounds having a wide spectrum of tumor activity. In the case of brain cancers alone, such a test is meaningless since it does not (and can not) determine if the compound can pass through the blood-brain barrier. Thus the testing described in the specification is not remotely commensurate with the literally hundreds of type of cancers affecting different organs (anal, bladder, breast, cervical, esophageal, eye, blood, liver, larynx, gallbladder, ovary, kidney testes, thyroid, brain, etc. and many different types for each) that is covered by the claim language even if test data was reported in the specification.

Also, note MPEP 2164.08(b) which states that claims that read on "... significant numbers of inoperative embodiments would render claims nonenabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative.". Clearly that is the case here.

Note substantiation of utility and its scope is required when utility is “speculative”, “sufficiently unusual” or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288. Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses.

Next, applicant's attention is drawn to the Revised Utility and Written Description Guidelines, at 66 FR 1092-1099, 2001 wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method treating solely based on the

inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. See Ragione et al., FEBS Letters 499. 199-204, 2001 especially concluding paragraphs which suggest further requirement for experimentation.

In evaluating the enablement question, several factors are to be considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Therapeutic use of the compounds in treating any or all cancer that require histone deacetylase inhibitory activity.

2) The state of the prior art: Recent publications expressed that the histone deacetylase inhibition effects are unpredictable and are still exploratory. See references cited above especially the concluding paragraph.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for treating any or all cancer with the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, “the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved”. See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples to show treating any or all cancer and the state of the art is that the effects of histone deacetylase inhibitors are unpredictable.

6) The breadth of the claims: The instant claims embrace treating any or all cancer with a huge genus of compounds by inhibiting histone deacetylase activity.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as “sufficient working examples”, “the level of skill in the art” and “predictability”, etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of enzyme-inhibitor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards treating any cancer based on mode of action of the instant compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP §2164.01(a) states, “A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was 'filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re

Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

This rejection is same as made in the previous office action but now excludes cancelled claim 14.

Applicants' traversal to overcome this rejection is not persuasive.

First of all, as noted above, instant claims, as recited, are reach through claims. A reach through claim is a claim drawn to a mechanistic, receptor binding or enzymatic functionality in general format and thereby reach through a scope of invention for which they lack adequate written description and enabling disclosure in the specification.

In the instant case, based on the inhibition of histone deacetylase by the instant compounds, instant claim reaches through treating any or all cancer in general and thereby it lacks adequate written description and enabling disclosure in the specification.

More specifically, in the instant case, based on the mode of action of instant compounds as inhibitor of histone deacetylase, based on limited assays, it is claimed that treating any or all cancer, in general, for which there is no enabling disclosure. It is not the breadth the claim it is the scope of enablement that is being addressed.

In the present case, specification has no objective enablement for any or all cancers mediated by histone deacetylase in general. Contrary to applicants urging, with the genus of compounds and large list of cancers, one trained in the art had to extensively undue experimentation.

Again to be more specific, instant genus would include millions of compounds. Representative examples of structurally diverse compounds generically embraced in the invention are not shown to possess in vitro activity much less in vivo uses claimed herein. Instant genus of benzamide compound embrace compounds with substituents bearing plethora of structural cores and functional groups and other groups permitted at instant variables which include variously substituted monocyclic rings, bicyclic rings, tricyclic rings with variable ring sizes and variable heteroatoms variety of reactive functional groups such COOH, OH ,SH, amido, sulfoxides, sulfones nitrile, carbamates etc. There is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same bioactivity profile since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for Markush group.

Again, it is not the objective enablement of genus of compounds is being addressed in the rejection. It is the scope of enablement for any or all cancers embraced in the claim language.

As for the traversal, again, applicants have not provided any direct evidence that the based on the mode of action of instant compounds, any or all cancers can be treated. Again, applicants' argument asserts the mode of action of the instant compounds as histone deacetylase inhibitors but there is no direct evidence presented to show any or all cancers can be treated because of the stated mode of action.

Applicants appear to assert that treating any or all cancers stated above with histone deacetylase inhibitors is known in the art but have not provided such a reference teaching treating all cancers with any such inhibitors. Since, search in the related art did not suggest such an assertion, applicants should provide the literature showing treating any or all diseases/disorders by kinase inhibitors.

Contrary to applicants' urging, given the large genus of compounds and large genus of cancers embraced in the claim language, one trained in the art need to unduly extensive experimentation without and then he need to assign the finding as applicants' invention for want of any guidance in the specification.

Applicants have not demonstrated nor have they alleged there is any correlation between the in vitro assays they disclosed in pages 20-22 and efficacy of treating against all cancers. In an unpredictable art, such as cancer therapy, in vitro assays may be used for enablement only if there is a well-established correlation between the assay and clinical efficacy.

The issue in Ex parte Balzarini 21 USPQ2d 1892 concerned HIV treatment and the Board of Patent Appeals and Interferences wrote "While the in vitro testing performed on these anti-viral compounds appears to be useful as a screening tool in order to determine which of these anti-viral compounds are candidates for further testing to determine if they possess in vivo utility, the in vitro tests were not predictive of in vivo efficacy."

The issue in Fujikawa v. Wattanasin 39 USPQ2d 1895 was adequacy of in vitro testing of inhibitors of cholesterol biosynthesis and U.S. Court of Appeals Federal

Circuit wrote, "in vitro results, in combination with a known correlation between such in vitro results and in vivo activity, may be sufficient to establish practical utility". Such a correlation does not exist in the art of cancer therapy employing CDK2 inhibitors.

In a peripheral issue involving assaying insulin-like growth factor-I ("IGF- I") in Genentech Inc. v. Chiron Corp. 55 USPQ2d 1636, U.S. Court of Appeals Federal Circuit wrote "by the critical date, ... [s]pecific binding in an RRA was known by those skilled in the art to be reasonably correlated with the in vivo biological activity of IGF-I."

In Ex parte Bhide 42 USPQ2d 1441, the Board of Patent Appeals and Interferences wrote "While in vitro or in vivo tests would not be the only possible way to overcome our basis for questioning applicants' utility, in vitro or in vivo tests certainly would provide relevant evidence". The issue in the present case is not the utility of applicants' compounds, which was at issue in Ex parte Bhide 42 USPQ2d 1441, but rather the narrower issue of enablement for claims drawn to the treatment of all cancers. Since such a claim is inherently not credible, the standard of proof required for such an assertion must be high.

In a case concerning a DNA sequence encoding a mature human IL-3 protein, Ex parte Anderson 30 USPQ2d 1866, the Board of Patent Appeals and Interferences wrote in passing "We question whether one skilled in the art would accept appellants' in vitro test as predictive of in vivo results and whether one skilled in the art would know how to use the Pro (8) protein made .... Should the claims of this application be prosecuted further in a continuing application we urge the examiner to consider the enablement and utility aspects of patentabilityi" In an anti-tumor application, Ex parte

Aggarwal 23 USPQ2d 1334, the Board of Patent Appeals and Interferences wrote "there is considerable doubt that those skilled in the art would be willing to accept appellants' in vitro tests and in vivo tests as established models predictive of utility against tumors in humans. See In re Jolles, 628 F.2d 1322, 206 USPQ 885 The examiner had more than adequate reason to doubt the objective truth of the broad statement of utility set forth in appellants' specification." In the most definitive finding on this issue of the adequacy of in vitro assays for clinical claims, Ex parte Stevens 16 USPQ2d 1379 the Board of Patent Appeals and Interferences wrote "The examiner's position is based on the supposition that the facts described above evidence a prima facie case of nonenablement with regard to the disclosed utility in light of all the applicable legal precedents. Where as here, the disclosed utility is the treatment of cancer, we agree with this supposition. The examiner has cited Ex parte Busse, 1 USPQ2d 1908. In that case, the Board of Patent Appeals and Interferences reviewed the relevant prior decisions of its reviewing court. We shall not repeat those citations here. Suffice it to say that in every cited case the narrow issue involved was whether or not the evidence of record was based on in vivo or in vitro studies which were generally recognized by those of ordinary skill in the art as being reasonably predictive of success in the practical utility under consideration, i.e., human or, at least, mammalian therapy."

In a vaccine case, Ex parte Maas 14 USPQ2d 1762, the Board of Patent Appeals and Interferences wrote "First, although appellants' specification describes certain in vitro experiments, there is no correlation on this record between in vitro experiments and a practical utility in currently available form for humans or animals. It is not enough

to rely on in vitro studies where, as here, a person having ordinary skill in the art has no basis for perceiving those studies as constituting recognized screening procedures with clear relevance to utility in humans or animals. The burden is on appellants to establish the significance of the in vitro experiments set forth in their specification."

None of the state of the art references cited above and cited in the specification expressed a single therapeutic approach for the treatment of all cancers embraced in the instant claim generally by administering a single class of compounds. Further, the state of the art not indicative of the fact that treatment of all types of cancer mediated by any kinase is conventional or well known. Moreover, the findings and conclusions in the cited publications with respect to inhibition of histone deacetylase and the application of such activity for specific types of cancers do not lend support for treating all cancers The instant claims, on the other hand, are drawn to several types of cancers affecting different organs and having different methods of growth or harm to the body, and different vulnerabilities.

However, the specification does not enable any physician skilled in the art of medicine, to use the compound of the invention commensurate in scope with the claims. The specification does not describe administration procedures and ranges of dosage regimen. The method of administration and/or the dose levels depend on a number of factors, which have to be evaluated by one of ordinary skill in the art. These factors include a) determining which of the claimed compounds would treat any particular claimed disease; b) synthesize the compound; c) formulate into a suitable dosage form depending the type of administration method; and d) conduct clinical trials or test the

compound in an assay known to be correlated to clinical efficacy of such treatment. The specification pages 20-22 provide three assays to determine the activity of the compounds and nothing more. Applicants have not asserted that it is art recognized that the assays are correlated to clinical efficacy for treatment of all indication mediated by any histone acetylase. There is no working example of treatment of any disease in man or animal. The state of the clinical arts in does not provide any agent which effective against all indication in general or those indication mediated by any or all kinase. Where the utility is unusual or difficult to treat or speculative, the examiner has authority to require evidence that tests relied on are reasonably predictive of in vivo efficacy by those skilled in the art. See for example In re Ruskin 148 USPQ 221; Exparte Jovanovics 211 USPQ 907.

In re Buting, 163 USPQ 689 (CCPA 1969) is on point and more applicable to the instant claims wherein 'evidence involving a single compound and two types of cancer, was held insufficient to establish the utility of the claims directed to disparate types of cancers. The judges in that case indicated that "We are not aware of any reputable authority which would accept appellant's two clinical cases as establishing utility for treatment of cancer in humans. As was pointed out in Brenner v. Manson, 148 USPQ 689, a process to be patentable must produce a useful result and be of substantial utility not merely of scientific interest or for further testing. In this case further testing seems necessary".

In summary, applicants have not provided any evidence of record that the instantly claimed compounds can effectively be used in the treatment of all cancers

mediated by histone deacetylase in general and therefore, it is maintained that one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Hence, this rejection is proper and is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-11, 16 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Delorme et al., WO 03/24448.

Delorme et al. teaches several histone deacetylase inhibitors, which include instant compounds. See page 26, formula 3 and note the definition of Cy^3, X^2 and Ar^3 groups. Especially note when X^2 = a chemical bond, with the given definition of Cy^3 and Ar^3, compounds taught by Delorme et al. include instant compounds. See pages 27-292for further details of the invention including various preferred embodiments, process of making and the examples of compounds made including various Tables for large number of species of compounds. Particularly see Table 5f, which include compounds of formula 3. Especially see compounds 238, 286-297, 301, 305, 353, 354, 355, 367, 465 and 466.

Delorme et al. differs from the instant claims in not exemplifying all compounds generically embraced in the formula 3 shown in page 26, especially those bearing piperidinyl group for Cy^3 (instant A ring choice). Instead Delorme al., teaches various heterocyclic groups as seen compounds 238, 286-297, 301, 305, 353, 354, 355, 367, 465 and 466.

However, Delorme et al. teaches equivalency of those compounds taught in Table 5f, pages 269-292 with those generically recited in for compound of formula 3 in page 26 and various other compounds..

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds using the teachings of Delorme et al. including the piperidinyl group for Cy^3 choice and expect resulting compounds (instant compounds) to possess the uses taught by the art in view of the equivalency teaching outline above.

This rejection is same as made in the previous office action but now excludes cancelled claim 14 and includes newly added claim 18.

It is also acknowledged that the correct Delorme reference is WO 03/24448 as recognized by the applicants. Though the content of the reference used is WO 03/24448, examiner had wrongly indicated WO 01/38322.

Applicants' traversal is not persuasive.

Contrary to applicants' urging, Delorme et al., provides teaching, suggestion and motivation make the genus of compounds taught therein. Particularly, there is teaching, suggestion and motivation to make instant compounds. Particularly see Table 5f, which include compounds of formula 3. Especially see compounds 238, 286-297, 301, 305, 353, 354, 355, 367, 465 and 466, which include instant compounds recited in the original claims with A ring as heterocyclic ring. Although instant claims exclude these compounds by election of piperidinyl group for ring A, Delorme et al., permits, pyridinyl group as a choice for heterocyclic group. See passage 0029, line 7. Hence, based on the teaching that compounds 238, 286-297, 301, 305, 353, 354, 355, 367, 465 and 466, which provides guidance to choose direct linking of heterocyclic group to the phenyl

ring, one trained in the art would be motivated to make compounds wherein heterocyclic group taught is replaced with the other heterocyclic groups including piperidinyl group which is positively recited in the preferred embodiment. caught in these examples. Such compounds are within the skill set of one trained in the art.

Hence, one trained in the art would be motivated to make various heterocyclic rings substituted benzamide permitted by the reference including those bearing a piperidinyl ring and expect these compounds have the use taught for the exemplified compounds.

Contrary to applicants' urging the subgenus of compounds embraced in these choices are small and one trained in the art would be able make and use these compounds for the said use.

As for applicants' argument that the genus of compounds embraced in the compound of formula I would exceed thousands of compounds, it should be noted that instant genus would exceed thousands of compounds with all the variable definitions. If instant specification provides guidance and motivation to make these compounds based on exemplified compounds, one should also give such credence to the genus of Delorme et al.

Also see KSR International Co. v. Teleflex Inc., 127 S.Ct. 1727 (2007), wherein the court stated that

[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has

good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

Such is the case with instant claims. Delorme et al., teaches generically a finite number of choices Cy^3 choices in the preferred embodiment. Hence, based on the teaching of compounds 238, 286-297, 301, 305, 353, 354, 355, 367, 465 and 466, which provides guidance to choose such a core, one trained in the art would be motivated to make compounds wherein the exemplified heterocyclic group is replaced with the any of the heterocyclic core positively recited in passage 0029 including piperidinyl group. Such compounds are within the skill set of one trained in the art.

Hence, this rejection is proper and is maintained.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-11, 16 and 18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims1-14 and 17-19 of copending Application No. 10/512,808. Although the conflicting claims are not identical, they are not patentably distinct from each other because the genus of compounds, process of making composition and the method of use embraced in the instant claims are also embraced in the claims 1-14 and 17-19 of the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

This rejection is same as made in the previous office action. Applicants' have differed addressing this rejection. For reasons stated above, this rejection is proper and is maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

/Venkataraman Balasubramanian/

Primary Examiner, Art Unit 1624